Crystalline Silica: Risks and Policy

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Since the International Agency for Research on Cancer labeled crystalline silica a probable carcinogen in 1988, government regulations have required sand and other products to contain warning labels and researchers have attempted to quantitatively assess low-exposure risks. The uncertainties are unlikely to diminish any time soon, and little value exists in calculating such risks, as low exposures to this ubiquitous mineral are commonplace in both urban and rural areas due to many uncontrollable activities. What is certain is that regulatory resources targeted at continuing high-level occupational exposures would be much more likely to have beneficial public health consequences than continued attempts to assess low-exposure risks quantitatively. *Key words*: International Agency for Research on Cancer, lung cancer, risk assessment, significant risk, silica. *Environ Health Perspect* 103:152–155 (1995)

U.S. public health officials and regulators have long been aware of the risks of crystalline silica. Certain high-exposure occupations using this ubiquitous material—whose most common form is sand—have caused serious, debilitating silicosis. More recently, concerns have been begun to be expressed about potentially wider risks to the general public from environmental exposure. A 1993 headline declared: "Cancer Scare: How Sand on a Beach Came to Be Defined as Human Carcinogen" *(1)*.

These concerns stem largely from lists of carcinogens published by the U.S. government or international groups. Once published, these lists trigger regulatory requirements—most significantly the requirement that listed substances be labeled as cancer hazards. Then, once warnings are displayed, a chemical becomes the subject of public concern, and, inevitably, fright. The 1993 *Wall Street Journal* article quotes a father reading a cancer label as he fills his child's sandbox: "Why am I letting my daughter play in something that says right on the label, it causes cancer?"*(1)*

Sand (quartz) is the most common form of crystalline silica, but this most abundant substance on the land surface of the earth is also found in a wide variety of minerals. Because of widespread natural occurrence, crystalline silica becomes airborne through both natural and anthropogenic forces. It is not surprising that airborne crystalline silica is commonly found in both urban and rural settings.

Once concerns were raised about crystalline silica, the response (as is common for many chemicals) was to assess the risks quantitatively to find out to what extent this "probable" carcinogen would really cause any cancer, among children in sandboxes, or anyone elsewhere. Employing the many tools of quantitative risk assessment (QRA) developed over the past 30 years, regulators attempted to determine how significant, if at all, is that risk.

Attempts to determine risks of low exposure to crystalline silica are still in their infancy. No QRA has to date been accepted by any government agency in the United States. This state of affairs should not, however, be cause for concern. The government and public will be ill-served by development of crystalline silica QRAs and debate about hypothetical risks of low exposures. Rather, public health experts should focus on the known target, namely, those workplaces where high silicosis-causing exposures are still occurring. As discussed here, the lack of utility of crystalline silica QRA emerges once one considers the very large uncertainties in, and the inadequacy of, the existing crystalline silica database for quantifying risks, and the fact that environmental exposures are ubiquitous. These factors argue against focusing regulatory attention on determining some low, "safe" exposure level.

Regulatory Background

In 1988, based on a 1986 working group conclusion that evidence of carcinogenicity, although limited in humans, was sufficient in animals *(2)*, the International Agency for Research on Cancer (IARC) included crystalline silica on its list of probable human carcinogens *(3)*.

The IARC classification triggered the U.S. Occupational Safety and Health Administration's (OSHA) Hazard Communication Standard (HCS) requirement that products containing more than 0.1% of any IARC-listed probable carcinogen be labeled as potential cancer hazards. The U.S. National Toxicology Program followed IARC's lead and, in 1991, also listed respirable crystalline silica as "reasonably anticipated to be a carcinogen," another event that triggers OSHA warning requirements.

Once listed, crystalline silica also faced regulatory scrutiny in California. That state's Proposition 65 warning requirements for the general public, like OSHA's for workers, are triggered by IARC or NTP listings. Moreover, California's air toxic "hot spots" rules can require firms releasing listed substances to assess fenceline risks so they can determine if they need to notify neighbors.

Both IARC and NTP declare their listings are but the first hazard identification step in risk assessment. As NTP puts it, "evaluation of the degree of potential human risk . . . requires a wider analysis" *(4)*. But, often no such "wider analysis" occurs before OSHA and California notification and warning requirements are triggered. The warnings, moreover (indeed as they are no doubt intended) raise public concerns that both industry and government often find necessary to address. Addressing those concerns has typically been achieved through quantitatively assessing risk.

Because sand had been labeled as "probably" carcinogenic to humans, and because it was felt necessary to tell the man filling his sandbox or the neighbor of a quarry whether he should be frightened by the labels, both California and the U.S. EPA began the QRA process. Before reviewing that process, it is necessary to summarize the crystalline silica health effects data available to attempt to quantify its risk at low exposure levels.

Scientific Background

As IARC found when it reviewed the crystalline silica literature, considerable data exist, but those data have many uncertainties and thus have been interpreted quite differently in the scientific community.

Crystalline silica has increased the number of lung tumors in several rat inhalation studies, but mouse, hamster, and guinea pig studies have not shown increased tumors *(5–9)*. And three of the rat studies, because they were designed as studies of compounds other than crystalline silica, administered only one dose, and thus there is no evidence of a dose–response relationship *(10–12)*. In the only two-dose rat study, lung tumor incidences were nearly identical, although silica doses varied fivefold *(13)*. As the senior

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investigator of one of the positive rat studies writes, "[t]here is plenty of evidence but a great deal of uncertainty about what it means" *(14)*.

Another expert in fiber toxicology has emphasized that great uncertainties exist in attempting to use animal findings to predict human risk given a "pattern which indicates that the rat lung responds to widespread chronic damage and fibrosis with tumor production much more readily than other species" (*15*). He concludes: "This makes the prediction of carcinogenic hazard to humans very difficult, because results from rats tend to exaggerate danger levels, particularly when extremely high doses are used" (*15*: p. 487).

The human data have their own uncertainties. Although there have been more than 50 worker epidemiology studies, few studies are available of cohorts defined by employment involving crystalline silica but not other potentially carcinogenic exposures. And, as is true in most epidemiology studies that focus on lung cancer, smoking could rarely be fully taken into account. Just as importantly, past silica exposure levels could only be approximated or ranked in an ordinal fashion, if exposure was estimated at all, in almost all studies. In addition, the type of crystalline silica, its chemistry and structure, has rarely been well-characterized in epidemiology studies.

IARC called the epidemiologic evidence as of 1986 "limited" *(2)*. The chair of the IARC panel emphasized shortly after crystalline silica's listing that the evidence for carcinogenicity of crystalline silica was "indeed limited" *(16)*. He thus noted that "although credible, alternative explanations such as chance, bias or confounding have not been adequately excluded. . . . Without more and better evidence it is premature to conclude that exposure to crystalline silica has caused lung cancer in man" (*16*: p. 290).

More than 30 epidemiologic papers considering the relationship between silica, silicosis, and lung cancer have been published since the IARC review. However, only about one-third of the studies are of reasonably satisfactory design and presentation and primarily concerned with the effects of crystalline silica exposure on lung cancer risk. Fewer than 10 studies provided some evidence of excess risk in exposed workers. Three papers provide results which, although individually unambiguous, are nonetheless as a whole inconsistent.

Merlo et al. *(17)* studied 1022 men employed 6 months or more manufacturing refractory bricks in Genoa, Italy. There were no obvious confounding exposures, but the role of smoking could not be assessed. By the end of 1986, 243 men had died, 28 from lung cancer [standardized mortality ratio (SMR) = 1.51; 95% CI, 1.00–2.18] and 40 from nonmalignant respiratory diseases (SMR = 2.41). There was some suggestion that risk in both these disease groups was highest in workers employed for 20 or more years before 1957 when dust controls were introduced, but no other indication of exposure dependency was reported.

Checkoway et al. *(18)* studied 2570 white male workers employed for one year or more mining and calcining diatomaceous earth in California, where the main exposure was to cristobalite. Possible confounding exposure from the earlier use of asbestos in some parts of the plant was considered by the investigators; cohort workers whose job titles were known to be associated with regular exposure to asbestos were excluded from the analyses. Additional information that came to light after the publication raises the possibility of more pervasive asbestos exposure to a substantial portion of the studied cohort.

By the end of 1987, of 628 observed deaths, 59 were from lung cancer (SMR = 1.43) and 77 from nonmalignant respiratory disease (SMR = 2.27). A semiquantitative index of cumulative dust and crystalline silica exposure was derived from work histories, differences in airborne concentrations, crystalline silica content of the products, era of employment, and respiratory protection. These were shown by regression analysis to correlate with relative risks for both lung cancer and nonmalignant respiratory disease. As judged by the limited information obtained on cigarette smoking, there was no indication of important confounding from this source.

The National Institute of Occupational Safety and Health (NIOSH) has updated a mortality study at the Homestake Mine in South Dakota *(19)*. Lung cancer mortality was not significantly elevated when national rates were used (SMR = 1.13; 95% CI, 0.93–1.36); there was marginal excess when county rates were employed (SMR = 1.27; 95% CI, 1.02–1.55). No positive exposure–response relationship was seen in contrast to the observed silicosis and tuberculosis, where overall excess and positive exposure–response gradients were observed.

Taken as a whole, the epidemiologic evidence on crystalline silica exposure per se inducing lung cancer in the absence of lung fibrosis must still be considered scanty and inconsistent, although biologically plausible. Of the eight positive studies, only one (*18*) showed a significant excess, evidence of an exposure gradient for risk, and reported absence of obvious confounders, and in this study the issue of asbestos confounding is being reevaluated. With the possible exception of the Homestake study (*19*), there is no study of comparable reliability to that of Checkoway (*18*) that has been negative. Resolution of this question will depend on further large cohort studies in which there are no important confounding exposures and where estimates of silica exposure are sufficient to demonstrate an exposure–response relationship, if present. Legitimate scientific debate exists as to whether crystalline silica causes cancer in humans. IARC may have concluded "probably," but other scientists equally familiar with the data say "maybe not."

No one disagrees that high exposures to crystalline silica have been definitively linked with silicosis; whether the same is true for cancer is not known. The extent to which any lung cancer risk associated with silica exposure is confined to those with silicosis cannot be answered at this stage. This could only be accomplished by a cohort study which can take into account exposure, silicosis, and smoking. Although studies using silicosis registries have raised the question of a link between lung cancer risk and silica exposure, they cannot contribute further to elucidating the realtionship because of the unquantifiable selection bias in compensated worker populations.

Even more problematic uncertainties exist if the crystalline silica data are to be used to assess risks quantitatively at low exposures. Which animal is most relevant to human assessment? How high were exposures in the past and (for risk characterization) how high are they today? Even more fundamentally, what was the particle size distribution and crystalline silica content of the dust? To what extent is duration, as opposed to intensity, of exposure important? Does age at time of exposure matter? To what extent is any evidence of increased lung cancer due to confounding by smoking? What about other substances to which studied workers were exposed? Does any cancer effect occur only above some threshold exposure? There can be no doubt that different risk assessors will reach different conclusions as to what these data mean.

Initial Quantitative Risk Assessments of Silica

Despite the absence of scientific agreement on whether silica causes cancer, the California statutory scheme, triggered by IARC, caused its regulators to attempt to quantify human risk. Warnings could be avoided under both the Proposition 65 and "hot spot" schemes if risks were found to be insignificant.

Using the positive rat studies, California's Department of Health and Human Services drafted a QRA that estimated lifetime exposures of 0.04–0.2 $\mu g/m^3$ posed a

10^{-5} lifetime risk (the California level for deeming a risk "insignificant") *(20)*. The authors, however, stressed that the apparent exactitude of the numbers was deceptive. They noted many uncertainties, including the inadequacy of, and inconsistencies in, the rat data, the negative findings in other species, and the possibility that any human cancer risk "may occur only after fibrosis (silicosis), a non-malignant disease, is induced" (*21*: p. 5). They concluded that their cancer predictions "may, therefore, be inappropriate" *(21)*. Uncertainties of the animal data were underscored by another assessment that found a 10,000-fold difference between cancer potencies predicted by two animal and two epidemiology studies (potencies ranging from 6.0×10^{-3} to 6.8×10^{-7} for lifetime 1 μg/m^3 exposures) *(22)*.

The California assessors also developed a preliminary noncancer, respiratory effects reference exposure level (REL) of 1.2 μg/m^3 by dividing the American Conference of Government Industrial Hygienists threshold limit value (ACGIH TLV) of 50 μg/m^3 by a time-adjustment factor of 4.2 and by a human intraspecies uncertainty factor of 10 *(25)*. Although California used 50, the current ACGIH TLV is 100.

Given the uncertainties admitted by its assessors, California has withdrawn both its cancer and silicosis risk assessments. The California EPA explained that the assessments were being "put on hold" until they could be peer reviewed and discussed with the public. The agency further noted that it did not "feel it is necessarily appropriate to use [such standards] as a basis for stringent regulatory action" *(23*: p. 2*)*.

California's uneasiness with its initial QRA attempts continued in an assessment conducted to determine whether local facilities needed to warn neighbors under the hot spots rules. The Monterey Bay Unified Air Pollution District found airborne crystalline silica levels near a quarry processing sand were 0.6 and 1.4 μg/m^3, but measurements in and around four other areas in the district (Salinas, Hollister, Santa Cruz, and King City) were higher: 1.4, 1.9, 2.3, and 1.4 μg/m^3, respectively *(24)*. The air board also commissioned a health evaluation to quantify cancer risk; it concluded that there was "too much uncertainty regarding cancer potency [values differing by a factor of 45,000] to make regulatory decisions."

At the same time California was backing off its QRA conclusions, the U.S. EPA also shelved its efforts to quantify noncancer silica risks. No doubt also sparked by the IARC listing, EPA's Air Office began receiving inquiries in the late 1980s about the safety of ambient silica. It thus began developing a reference concentration (RfC), using its standard "safety margin" assumptions to identify a level so low that EPA could conclude no risk existed. Those initial efforts pinpointed levels of 0.03–2.0 μg/m^3. But EPA backed off these tentative RfC calculations. Noting that crystalline silica is a "complicated public health issue," EPA's assistant administrator of research and development wrote in early 1993 that the agency had not yet decided whether to issue an RfC. EPA put off any issuance until it reviews, in several years, the National Ambient Air Quality Standard for particulate matter *(25)*.

In summary, both the U.S. EPA and California halted their initial efforts to quantify crystalline silica risks. Initial attempts to set "safe" exposure levels for both nonmalignant and malignant respiratory effects have been admitted to have been so uncertain, despite the apparent precision of the calculated numbers, that they should not be credited.

The regulators are likely to face pressures to employ their QRA apparatus again. Indeed, California is doing so. As discussed below, public policy would be well-served if the machinery remains idle. As one 1990 review of crystalline silica concluded: "Caution is required but caution runs both ways. Current evidence should not drive us inextricably toward overly stringent regulation" *(14*: p. 235*)*.

A Common-Sense Program

QRA may be an effective tool for policy decision-making on potential health risks, depending on the appropriateness of the model and the completeness of the relevant scientific database. It also depends on whether a significant risk to the population being protected is likely to be present and if any such risk can be mitigated. The thesis here is that public health would best be served by focusing resources on ending high occupational exposure and forsaking further crystalline silica QRA efforts to define low, safe levels.

More than uncertainty, however, should cause public health officials to stop any QRA momentum. First, it is becoming increasingly clear that most human crystalline silica exposure occurs from sources that cannot, and never will be, controlled. Second, much work needs to be done to eliminate high exposures to crystalline silica in some poorly controlled workplaces.

Crystalline silica all around us. Extensive analyses of ambient air to determine crystalline silica concentrations have not yet been conducted. What data do exist indicate that concentrations in the 1–10 μg/m^3 range—well above the preliminarily calculated safe levels—are common in both urban and rural settings.

A recent summary of eight monitoring studies concluded that the "average ambient crystalline silica" level was 6 μg/m^3. The authors noted that these values reflected the consequences of both anthropogenic agricultural activities and natural forces while "nearby industrial activity . . . contributed only slightly to the crystalline silica within the samples collected" *(26*: p. 7*)*. As noted above, the Monterey Bay study also found a quarry unlikely to be contributing to ambient levels.

Pausing to consider the importance of such ambient levels seems wise given the mistakes (now admitted by EPA) that were made with asbestos in buildings. EPA was quick in 1982 to predict, based on QRA, that up to 40,000 schoolchildren a year would die of cancer because their schools contained asbestos building materials. But, by 1988, the agency got around to measuring exposure levels in those schools and found airborne asbestos levels were no different indoor than out. As a result, the EPA admitted that it had unfortunately encouraged unwarranted and undesirable asbestos removal. It also helped to generate needless fear in parents regarding putative health risks to which their children were subjected.

Learning from the asbestos error is important to crystalline silica. Whatever the quantitative risk of lifetime exposures to crystalline silica may be, those risks have been experienced by humans for centuries and will continue in the future. As one crystalline silica risk assessor concluded: "There is the possibility that costly emission controls may be required that do little to reduce public lung cancer risk" *(22*: p. 29*)*. Continued QRA exercises are unlikely to be of any meaningful value to regulators and would likely serve only to raise concerns among those unwilling to tolerate any risk.

The crystalline silica that should be controlled. In contrast to the low crystalline silica concentrations all around us are the high exposures (above the OSHA 100 μg/m^3 permissible exposure level) being reported in certain inadequately controlled workplaces. The need to address these exposures, especially in some sandblasting and rock-drilling occupations, has become a focus of concern for NIOSH *(27)*. OSHA's Advisory Committee on Construction Safety and Health has also called for more attention to such workplaces *(28)*.

As NIOSH has emphasized, the issue is not assessing hypothetical risks or having OSHA issue a QRA to justify reducing the permissible exposure level. Rather, resources are needed to end already unlawful practices. An Australian public health official similarly concluded after conducting a silica

QRA: "It is unlikely that a reduction in the exposure standard will affect the overall number of silicosis cases without a subsequent change in approach to enforcement and self-compliance" *(29*: p. 11*)*.

Industry has been criticized for using QRAs to demand precision in assessing risks. It has been advocated that, instead, "What we should be doing is looking more closely at the distribution of death and disease, and then asking what portion can be prevented" *(30*: p. 406*)*. Focusing on eliminating high-exposure workplaces that may be contributing to development of silicosis provides a clear path to such prevention.

The ability of regulatory agencies to deal effectively with chemical hazards is limited both by staff and by the need to respond to public concerns. Further work on crystalline silica QRAs is unlikely to be a valuable use of staff time or worthwhile for regulatory program development. Indeed, QRAs, given all their uncertainties, are likely only to raise concerns that cannot be addressed.

More significantly, any search for the virtually safe exposure is likely to divert resources from actions to end identifiable workplace violations. Society may not know, and may never know, if the crystalline exposures it cannot avoid pose health risks of any consequence. Society does know it can and should end workplace exposures known to cause silicosis. Resources should be focused on that task.

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